REMARKS

Phone Interview

Applicants thank the Examiner for his time spent in discussing proposed amendments to the claims to overcome the obviousness rejections. Examiner suggested amending the claims to include the limitation that the immunogenic composition is formulated for local administration directly to a mucous membrane.

Status of the Claims

Claims 24-36 are currently pending in this application. Claims 1-23 have been canceled without prejudice or disclaimer of the subject matter therein. New claims 24-36, drawn to the same invention as claims 15-20, have been added. Thus, claims 24-36 are currently under examination.

Rejoinder of Process Claims

MPEP 821.04 provides that once a product claim is found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined. Thus, once a product claim is found allowable, Applicants will present process claims that depend from or otherwise include all the limitations of the allowable product claim. Applicants respectfully point out that process claims were originally presented in the present application, but were cancelled because the process claims did not depend from or include all the limitations of an allowable product claim.

Amendments to the Claims

Support for new claims 24-36 is provided in the Table below.

Claim	Support
24	Original claims 15, 17 and 22;
25, 26, 27	Original claim 16
28	Claim 17
29	Original claim 18
30	Original claim 19
31	Original claim 23

32	Page 13, lines 4-11 and page 16, lines 3-19
33	Page 3, lines 16-21
34	Page 6, lines 6-11
35	Page 6, lines 6-11
36	Page 6, lines 12-15

Rejection Under 35 U.S.C. § 103(a)

Claims 15-20 and 23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lavallee *et al.* in view of Alving *et al.*

Claims 21 and 22 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lavallee *et al.* in view of Alving *et al.* and further in view of Mannino *et al.*

Claims 15- 23 have been canceled without prejudice or disclaimer of the subject matter claimed therein. The limitations of claim 22 have been incorporated into new claim 24. Claims 15-23 have been replaced with new claims 24-36. Claims 24-36 are directed to an immunogenic composition formulated for local administration directly to a mucous membrane comprising a recombinant HIV-1 envelope protein comprising a mutated V3 loop, wherein the mutated V3 loop comprises the GPGRAF (SEQ ID NO: 1) hexamer sequence flanked by two basal cysteins but lacks all or a portion of the rest of the V3 loop, said recombinant HIV-1 envelope protein being anchored onto preformed liposomes. The claimed invention is based on the unexpected discovery that modifying the V3 loop of HIV-1 envelope protein by deleting all or a portion of the V3 loop except SEQ ID NO: 1 produces an immunogen that induces humoral immunity (neutralizing antibodies), cellular immunity (cytotoxic T-lymphocytes), and mucosal immunity (production of secreting an nuetralizing IgA) against divergent strains of HIV-1.

Since the limitations of claim 22 have been incorporated into new claim 24, claims 24-36 are not obvious over Lavallee *et al.* in view of Alving *et al.* or over Lavallee *et al.* in view of Alving *et al.* and further in view of Mannino *et al.* for the reasons set forth below.

The attached declaration by Dr. Luc Montagnier, an expert in the field of virology, specifically in the field of retroviruses including HIV and vaccines against HIV, establishes that the claimed invention is not obvious over the cited references. Briefly, the declaration attests that the claimed composition has an unexpected property of inducing humoral, cellular, and mucosal immunity against divergent strains of HIV-1. The declaration attests that the claims are not

obvious over Lavallee *et al.* in view of Alving *et al.*, and that the claims also are not obvious over Lavallee *et al.* in view of Alving *et al.* and further in view of Mannino *et al.* The cited references do not provide the motivation to modify the disclosed composition of the cited references to obtain the claimed invention. The deficiencies of the cited references are discussed below.

Although Lavallee *et al.* disclose the expression and characterization *in vitro* of recombinant HIV-1 gp160 Env proteins in which the V3 loop is partially (envΔ3-GPGRAF) or totally (envΔ3+) deleted, Lavallee *et al.* neither describe nor suggest the use of the modified glycoprotein in an immunogenic composition for local administration to the mucous membrane. The goal of Lavallee *et al.* in modifying the V3 loop was to induce broadly reacting neutralizing antibodies capable of neutralizing divergent HIV-1 isolates. Moreover, the cited reference does not teach immunogenic compositions comprising a modified HIV-1 glycoprotein capable of inducing a humoral immunity, a cellular immunity and a mucosal immunity against divergent strains of HIV-1.

Alving *et al.* disclose inducing an immune response to an antigen via a transdermal route on intact skin. However, Alving *et al.* do not teach local delivery of an immunogenic composition comprising a modified HIV-1 glycoprotein to a mucous membrane. In fact, Alving *et al.* suggest that the preferred route of administration of an antigen is subcutaneous injection or transdermal, since Alving *et al.* state that topically applied formulations of antigen and liposomes do not induce an immune response equivalent to that induced by subcutaneous injection (col. 1, lines 60-67) and that for the majority of vaccine applications using liposomes, the formulations are injected through the skin with a needle. Thus, Alving *et al.* provide no motivation for local delivery of a modified HIV-1 glycoprotein directly to the mucous membrane.

Mannino *et al.* teach immunogenic compositions comprising a nonimmunogen peptide and at least a lipid, but do not teach local delivery of immunogenic compositions comprising modified HIV-1 glycoprotein to a mucous membrane. The composition of Mannino *et al.* is only able to induce selective antibody production against a non-immunogen peptide. The nature of the peptide in the composition of Mannino *et al.* appears to be the factor determining the structure that results. That is, those peptides that are hydrophilic or neutral appear to more often form vesicular structures, whereas those that are amphipathic appear to more often form amorphous, particulate aggregates.

Moreover, although Mannino *et al.* provide general guidance that the dosage form can be oral, nasal, intravaginal or on any mucosal surface (col. 13, lines 31-33), there is no specific guidance for effective local delivery of a modified HIV-1 glycoprotein to a mucous membrane to induce humoral, cellular, and mucosal immunity. Given the long history of attempts to produce useful vaccines which produce an effective immune response to HIV, references which only generally speak of possible vaccine formulations are only invitations to experiment or obvious to try. However, without more specific guidance from the cited references for obtaining a deliverable modified HIV-1 glycoprotein, the cited references do not render the claimed immunogenic compositions obvious because there is no expectation of success in obtaining and delivering the claimed immunogenic compositions in a manner effective to induce all three forms of immunity.

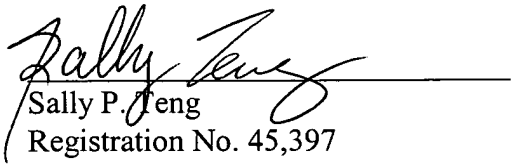
In summary, the declaration sets forth the reasons that the cited references do not render the claimed invention obvious. Lavallee *et al.* neither describes nor suggests the use of a modified HIV-1 glycoprotein to make immunogenic composition for local delivery to a mucosal membrane. The deficiencies of Lavallee *et al.* are not corrected by Mannino *et al.* or Alving *et al.* because neither of these references suggests that mucosal route could be effective for HIV-1 delivery. Applicants respectfully request withdrawal of the rejection.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, they are invited to telephone the undersigned at their convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
Morgan, Lewis & Bockius LLP



Sally P. Teng
Registration No. 45,397

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Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Tel: 202-739-3000
Fax: 202-739-3001